(54) Title: CONTACT LENS COATING SELECTION AND MANUFACTURING PROCESS

(57) Abstract: The invention is a method of making a coated contact lens with desirable physiological performance. Preferably, the lenses are made from hydrophobic contact lens substrate with a hydrophilic coating material. The hydrophobic lens substrate is coated with a hydrophilic material having an expansion factor greater than one. The coated lenses have low physical defect and surface roughness profiles.

CONTACT LENS COATING SELECTION AND MANUFACTURING PROCESS

5   ## BACKGROUND OF THE INVENTION

This invention relates to contact lenses. More particularly, it relates to contact lens substrates made of one material and coated with another and methods for selecting and preparing such combinations to achieve good physiological performance of the coated lenses.

10   Coating a substrate of one material with a different material has been proposed as a strategy for making contact lenses for a variety of reasons. The coating may offer a property or properties that are different from those of the substrate and which are particularly desirable as a lens surface apart from the bulk properties of the lens material itself. Properties such as wettability, resistance to

15   proteinaceous deposits, biocompatability, UV shielding and other desirable lens characteristics and properties could conceivably be addressed with this approach.

US Pat. 5,779,943, for example, proposes preparing a molded article such as a contact lens by coating a bulk polymer with a latent hydrophilic material in the mold. The molded article is made more wettable at its surface. WO 96/24392 to

20   Morra, et al., proposes coating a substrate with hyaluronic acid to improve biocompatability. One proposed use for the coated substrate is in intraocular lenses. WO 94/06485 proposes coating a hydrophobic substrate with a carbohydrate to make the device from which it is made more wettable at its surface. WO 93/00391 proposes coating a hydrogel with a hydrophilic coating polymer to make the

25   substrate more hydrophilic and less prone to adhesion by tear proteins. US Pat.

5,708,050 proposes coating a lens substrate with a silicone oil, a polysaccharide, or a denatured collagen to make it more hydrophilic at its surface. Beyond a general recognition that wettability and oxygen permeability are desirable lens characteristics, little insight has been provided on substrate/coating selection and

5   application criteria for physiological compatibility. That is, there has been little guidance available for determining substrate and coating materials and application conditions that will provide good physiological performance.

Simply coating a lens substrate made from hydrophobic monomers with a hydrophilic coating material without accounting for such critical parameters will not

10   alleviate the problems such as dryness and surface deposition described above. It has not been possible to predict the success of a given lens/coating combination or coating process until lenses made from the material were placed in actual physiological conditions. Thus, materials that have appeared to provide favorable properties have often manifested the negative conditions described above only when

15   actually placed in contact with a wearer's eye. This has left the selection of suitable coated contact lens materials and coating methods largely an empirical art with little ability to predict even the physiological effect of lot to lot variations in contact lens manufacturing processes.

Polymers made from silicones and other hydrophobic materials (e.g.,

20   polyfluorinated polymers and polypropylene glycol) used as contact lens materials present particular challenges that might be addressed with coating processes. The oxygen permeability of such lens materials can be very high making them desirable in many instances. However, the surfaces of such materials typically do not provide desirable levels of wettability. This, among other properties of lenses made from

25   hydrophobic materials can result in dryness, grittiness, and general discomfort. The

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surfaces of such polymers also tend to have an affinity for certain tear components

such as proteins, lipids and mucin. This can result in increased surface deposition

and fouling with opaque deposits when worn. Such lenses can also become tightly

adhered to the cornea, potentially leading to serious damage to the corneal

5   epithelium. Plasma coating processes, aqueous and organic coating processes, and

surface derivitization have all been described as potential methods for coating the

hydrophobic lens material or changing its wettability at the surface.

The field of contact lens production could benefit greatly from a predictive

method for selection and production of materials without undue reliance on testing

10   in physiological conditions. While one cannot eliminate such testing, better

predictive models will streamline materials selection processes by reducing the

number of different options to be tested. They would also provide a means for

distinguishing useful and beneficial materials combinations and lenses from

materials combinations and lenses that are not so useful or beneficial during

15   manufacturing and testing of lenses.

BRIEF SUMMARY OF THE INVENTION

The invention is a process for coating a contact lens substrate with another

material to achieve desirable physiological performance. In one aspect of the

20   invention, the substrate is coated with coating that will have a surface area expansion

factor greater than one. The coated lenses have low physical defect and low surface

roughness. Preferably, they have a sub-micron coating thickness.

In another aspect of the invention, a lens substrate made from hydrophobic

monomers is coated with a hydrophilic material having a surface area expansion

25   factor greater than one.

In yet another aspect of the invention, a method of coating a contact lens

comprises selecting a lens substrate material, selecting a coating material which will

have a surface area expansion factor greater than one relative to the lens substrate

material, coating the lens substrate material with the coating material, and forming

5   and selecting coated lenses having low physical defect and surface roughness

profiles.

DETAILED DESCRIPTION OF THE INVENTION

Good physiological performance is obtained in coated lenses made according

10   to this invention. For the purposes of this specification, good physiological

performance or physiological compatibility is marked by a lens which when in

contact with the eye results in good clinical comfort (average comfort > 40 on 50

point subjective scale), good wettability (non-invasive tear break up time

(NIBUT)>5 sec), minimal corneal disruption (average maximum type corneal

15   staining ≤ 1), and minimal on-eye lens spoiling (average deposits ≤ slight). A lens

that meets these criteria is a physiologically compatible contact lens as the term is

used throughout this specification.

Virtually any substrate that can be fashioned into a contact lens can be used

in this invention provided it is optically transparent and is oxygen permeable.

20   Suitable substrates include polymers made from hydrophobic materials such as

silicone copolymers, interpolymers, oligomers, and macromers. Illustrative

polysilicones are polydimethyl siloxane, polydimethyl-co-vinylmethylsiloxane.

Other silicones are the silicone rubbers described in U.S. Pat. No. 3,228,741 of

Becker issued Jan. 11, 1966; blends such as those described in U.S. Pat. No.

25   3,341,490 of Burdick et al., issued Sept. 12, 1967 and silicone compositions such as

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described in U.S. Pat. No. 3,518,324 of Polmanteer, issued June 30, 1970.

Substrates described in US Pat. No. 4,136,250; 5,387,623; 5,760,100; 5,789,461;

5,776,999; 5,849,811; 5,314,960 and 5244,981 are also particularly suitable for use

in this invention. Cross-linked polymers of propoxylate of methyl glucose and

5   propylene oxide and HEMA-based hydrogels are different classes of substrates

amenable to the process of this invention.

Preferred silicone compositions useful in forming the substrate of this

invention are the cross-linked polysiloxanes obtained by cross-linking siloxane

prepolymers by means of hydrosilylation, co-condensation and by free radical

10   mechanisms such those described by Chen in US Patent 4,143,949 which is

incorporated herein by reference. More preferred silicone-based substrates are

cross-linked polymers of α,ω-bisamionpropyl polydimethylsiloxane, and gylycidyl

methacrylate, cross-linked polymers. The particularly preferred substrates are

silicone compositions that are made from combining a methacrylate one or more

15   silicone monomers in the presence of a Group Transfer Polymerization catalyst to

form a macromer that is subsequently polymerized with other monomers to give the

final substrate. Initiators, reaction conditions, monomers, and catalysts that can be

used to make GTP polymers are described in "Group Transfer Polymerization" by

O.W. Webster, in Encyclopedia of Polymer Science and Engineerig Ed. (John Wiley

20   & Sons) p. 580, 1987.

·The coating selected must be capable first of adhering to the substrate. This

can be via chemical bonding such as covalent or ionic bonding or it can be via

physical attraction so long as the coating can be made to adhere to the substrate.

That is, the coating must be capable of remaining affixed to the lens substrate

25   throughout its useful life (storage time plus the time in which it will be in contact

with a user's eye). It is also possible to use more than one layer of coating. This is

particularly desirable where the coating layer will provide the requisite surface

properties (as described more fully below) but is not particularly compatible with the

substrate by itself. For example, a tielayer or coupling agent can be used to adhere

5   the hydrophilic coating to the substrate. A coating layer with a significant number

of carbonyl groups could be bonded to a polyolefin substrate through the use of a

diamine tielayer in such a scheme. Selections of compatible lens substrate, coating,

and tielayer (if necessary) materials is well within the knowledge of one skilled in

the art.

10   Mere adhesion is not enough to produce the coated lenses of this invention.

.The coating material must be one that will exhibit a surface area expansion factor

greater than one relative to the lens substrate. The coating surface area expansion

factor, as the term is used throughout this specification, is the fractional expansion of

the coated lens surface area due to the coating as the lens goes from the coating

15   condition to the final physiological saline solution. The expansion factor is arrived

at by measuring the increase in surface area of the lens as a result of the coating

when taken from the coating condition to a physiological buffer. In practice this can

be directly measured by determining the fractional increase in surface area due to the

coating using atomic force microscopy (AFM). For example, the true surface area in

20   an arbitrary AFM scan area can be determined for the coated article (under

physiological conditions) and the uncoated article under coating conditions. The

ratio of these measurements is defined as the coating expansion factor. Using a 20 X

20 μm scan area we might find that the true coated surface area is 412 μm^2, while

the true surface area of the uncoated lens is 400.8 μm^2. The surface area expansion

25   factor ratio of the coating is 1.0279.

Parameters such as pH, temperature, ionic strength, and dielectric constant of the coating solution can all be used to select and combine materials which will display the proper relative expansion condition of the substrate and coating in a particular set of conditions (within certain ranges dependent upon the materials

5   considered). For example, ionic coating polymers (and/or lenses) can change volume dramatically with pH. Thus a pH can be chosen to shrink the coating relative to the substrate during the coating process.

Alternatively, the coating conditions can be arranged such that the lens substrate is highly swollen. This can often be controlled using temperature or by

10   changing the dielectric constant of the coating solution. Organic solvents can be particularly useful for silicone hydrogel lens substrates where the lenses often swell by a factor of two or three in solvents such as isopropanol, ethanol, acetonitrile, tetrahydrofuran. Very hydrophilic coatings will not swell so dramatically under those conditions. Also, it is possible to apply the coating to a hydrated lens as a

15   solid, low water content paste. Combinations giving an expansion factor greater than 1.00 are preferred with combinations giving expansion factors greater than 1.01 being most preferred. Acceptable coatings can have expansion factors greater than 1.03 and still be within the scope of the invention. However, coatings cannot be used where such a high surface expansion factor contributes to surface roughness

20   beyond that described as acceptable in this specification.

Combinations of coating materials and lens substrate materials that will result in an expansion factor greater than one include, for example, non-ionic silicone hydrogel substrates with water content between 20 and 50% and anionic coating polymers such as polyacrylic acid ("PAA"), poly(methacrylic acid),

25   poly(itaconic acid), poly(maleic acid), poly(sulfopropyl methacrylate sodium salt)

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and block or random copolymers of those acid monomers (coating done at low pH).

Also, non-ionic silicone hydrogel lenses with non-ionic polymer coatings such as:

polyacrylamide, polydimethacrylamide, polyvinylalcohol, cellulose, dextran,

polyethylene oxide.

5   The coatings are applied at the submicron level (between about 0.1 nm and

500 nm thick). They are prepared and applied as aqueous solutions, suspensions, or

colloids and then applied to the substrate according to any process that will put the

coating in uniform contact with the substrate. For example, immersion, spraying,

brushing, and spin coating are all useful application techniques. Immersion and

10 spraying are the preferred processes since proper thickness and uniformity of the

coating are most easily accomplished with them. In the most preferred embodiment,

coating thickness at the submicron level is achieved by preparing a dilute polymer

solution of coating material such as a solution between about 0.1 and 6.0 wt% of

PAA. A silicon-based polymer substrate is then immersed in it for between 1 min

15 and 120 minutes at temperatures of 5-80 °C followed by a five step rinse over

approximately 30 min in which the unreacted polymer is washed away using a

buffered saline solution.

The process must also leave the coating with a low physical defect profile. A

low physical defect profile, as the term is used throughout this specification, means

20 that once coated, the coating layer has no physical defects such as holes or tears that

are greater than 4.6 μm across along the longest dimension of the defect. Holes or

tears less than 4.0 μm are preferred with those less than 0.5 μm most preferred. This

parameter can be met by applying the coating under conditions sufficient to reach

confluence and by ensuring that all parts of the lens substrate are exposed to

25 essentially equivalent coating conditions. For example, the process must require

that the coating material itself and all activation elements (e.g., crosslinkers,

catalysts, and initiator) are uniformly distributed when averaged over time.

Processes that require contact between a tool, mold piece or the like and a portion of

the lens during coating will not generally meet this criteria. Solution coating

5   processes in which the lens substrate is freely floating and the coating solution is

isotropic and not diffusion limited are most preferred. Additionally, no debris or

dust should attach to the lens, so that a homogenous surface is formed to which the

coating may adhere defect free. This surface homogeneity requirement also means

that any phase separation (domains) on the lens must be smaller than 4.6 μm in

10   dimension. In the aspect of this invention that involves the selection of coating

materials, this criteria will preclude the use of polymers known to form voids or

spherulites greater than 4.6 μm.

In the aspect of the invention in which coated substrates meeting this

requirement are selected for use and those not meeting this criteria are discarded, any

15   method for detecting surface defects of this size can be employed. Such methods

can include, for example, Atomic Force Microscopy (AFM), stylus and optical

profilometry, and electron microscopy including Scanning Electron Microscopy.

In addition to providing the coated lens substrate with a low defect profile,

the process must also imbue the coated substrate with a low surface roughness

20   profile. A low surface roughness profile, as the term is used throughout this

specification, is a peak to peak surface roughness of less than 475 nm over any 10 x

10 μm area on the surface of the coated lens substrate. Peak to peak roughness is

defined as the difference between the highest peak and lowest valley in a 10 X 10

μm image area. This criteria is met by ensuring smooth molds and smooth uncoated

25   lens substrates as well as controlling the amount of coating applied to the lens (as

described above) so that it does not create excessive roughness of the surface. US patents 4,565,348 and 4,640,489 describe methods of making molds meeting these requirements. Both patents are incorporated herein by reference.

In the aspect of the invention in which coated substrates meeting this

5   requirement are selected for use and those not meeting this criteria are discarded, any method for detecting surface roughness of this magnitude can be employed. Such methods can include, for example, AFM, light scattering such as that performed with the Goniometric Optical Scattering Instrument (GOSI), direct optical microscopy, and environmental scanning electron microscopy. Methods amenable to automated

10 inspection systems during manufacture are preferred. The optical microscopy method is preferred in a manufacturing setting if the optical microscopy is capable of observing the coating uniformity. This method can be readily automated so that coated lens substrates can be automatically inspected and selected for use or discarded based on a programmed command using the selection criteria for surface

15 roughness described above.

The aspect of the invention in which coated substrates having coatings with a surface area expansion factor greater than one (relative to the lens substrate), the coating has a low defect profile, and a low surface roughness profile are selected for use and those not meeting this criteria are discarded, the process is conducted as

20 follows.

A lens substrate and coating combination are selected as described above. A lens substrate is formed from the material selected for its use using any known method for forming such substrates. The process described in US Patent 4,245,069 (incorporated herein by reference) is suitable for this purpose. The lens substrate is

25 then coated with the coating matched to substrate material so that it will have a

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surface area expansion factor greater than 1 as described above. It is preferred that the coating is adhered to the substrate by contacting an aqueous solution of the coating to the substrate such that the coating is bonded. Covalent bonding is preferred. Once the lens substrate is coated it may be subjected to any number of

5   additional steps that are conducted in the manufacture of contact lenses. These can include, for example, swelling and washing steps, the addition of additives such as surfactants, extraction steps and the like.

At a point after the coating is adhered to the lens substrate and preferably after any intermediate steps just described, the lens can be subjected to inspection for

10 physical defect profile, roughness profile, or both. This can be facilitated and automated by preparing the coating with a stain, preferably before coating the substrate with the coating material. Those lenses found to meet the selection criteria proceed to packaging for commercial distribution and those that do not are discarded (i.e., not further processed for commercial distribution).

15 Alternatively, one can take a statistical approach to the selection process. This is done by identifying a statistically relevant population of lens within a prescribed unitary portion of the lenses produced (e.g., a commercial lot) and analyzing a number of lenses sufficiently representative of the population so that one can be sufficiently confident that all members of the population have the prescribed

20 physical defect and surface roughness profiles. Those populations having such criteria are then selected for commercial use. Those populations for which such confidence cannot be displayed are either discarded or subjected to further evaluation to determine whether some portion thereof can be selected for commercial use. When this alternative is used, a confidence level of 83% for surface

roughness and/or physical defect profile is required. A confidence level of at least

98% is preferred.

The invention will be further described by the following nonlimiting

examples.

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EXAMPLES

Example 1: Substrate Formation

12.5 g KOH were added to 350 g of 20 mole propoxylate of methyl glucose,

available from Americol Corp., Edison, N.J. as GLUCAM™ P-20, in a high

10   temperature/pressure reactor. The mixture was heated to 105° C, stirred for 30

minutes with nitrogen sparging, and then pulling vacuum. After repeating the

sparge/vacuum two more times, the pressure was allowed to rise to 10 psi and the

temperature increased to 125° C. 1922 g propylene oxide were added gradually over

7 hours while maintaining a pressure of 30-40 psi and a temperature of 135° C.

15   After continuing agitation overnight, 947 g ethylene oxide were added following a

similar procedure. The product was neutralized with 9.1 g phosphoric acid and

filtered with dicalite to give a slightly hazy liquid with a hydroxyl number of 28.3

mg KOH/g

To a solution of 200 g of this product, 21.0 g triethylamine and 342 mg N,N-

20   dimethylaminopyridine in 600 g dry ethylene glycol dimethyl ether at 40° C were

added 32.1 g of methacrylic anhydride in 250 g ethylene glycol dimethyl ether

dropwise to the reaction flask over a 7 to 8 hour period. The reaction was continued

at 40° C for 7 days.